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10/663,010	09/15/2003	Tim Clarot	33205.0800	1757

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EXAMINER	
ALSTRUM ACEVEDO, JAMES HENRY	
ART UNIT	PAPER NUMBER
1616	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/663,010	CLAROT ET AL.	
	Examiner	Art Unit	
	JAMES H. ALSTRUM ACEVEDO	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30,31 and 40-57* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30-31 and 40-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 30-31 and 40-57 are pending. Applicant previously cancelled claims 1-29, and 32-39. Receipt and consideration of Applicants' claim amendments, terminal disclaimer, and remarks/arguments, submitted on July 30, 2008 are acknowledged. All rejections not explicitly maintained in the instant office action have been withdrawn per Applicants' claim amendments.

Terminal Disclaimer(s)

The terminal disclaimer filed on 7/30/08 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of U.S. Patent No. 7,115,275 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Claim Interpretation[1]

At the outset, the following claim interpretation is set forth so that the grounds of rejection hereinafter can be better understood. There is one independent claim and many dependent claims in the instant application that explicitly describe the **composition viscosity**:

- wherein the composition has a viscosity of about 2,500 cp and to about 40,000 cp (independent claims 30-31, 41, and claims dependent therefrom).

The one thing that stands out about applicant's choice of claim language is that the viscosity numbers are provided without a temperature parameter. Viscosity of a fluid is of course known to change with temperature. Common experience of every person who has spent any time in the kitchen is that a fluid such as a hot sauce, chocolate melt or gravy thickens

(viscosity increases) when cooled (as temperature decreases). McGraw-Hill Encyclopedia of Science & Technology discloses, inter alia, that the viscosity of glycerin1 at 0°C is 12,110 cp, and MacMillan Encyclopedia of Physics discloses that the viscosity of glycerin changes dramatically as the temperature increases: 830 cp (20°C), 0.16 cp (40°C) and 0.044 cp (60°C). Hence, within a temperature difference of 60°C, viscosity of glycerin can change by a factor of 275,227.

Plainly, viscosity of a fluid cannot have a fixed meaning without its temperature. Therefore, applicant's failure to specify a temperature for the claimed viscosity feature is interpreted as leaving open the viscosity as a feature that can exist at any temperature. For example, glycerin per se would meet all of applicant's claimed viscosity feature language as set forth above, because it inherently does possess a viscosity within 2500-40,000 cp since its viscosity at 0°C is 12,110 cp.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 41-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 41-46 recite the limitation "the viscosity" in line 1 of said claims. There is insufficient antecedent basis for this limitation in the claim.

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[1] This claim interpretation is also applied to copending applications and commonly owned U.S. Patents cited below

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 30-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haslwanter et al. (U.S. Patent No. 6,565,832) in view of Sundgreen et al. (U.S. 2002/0147232).

Applicant Claims

Applicants claim a composition for application to a nasal membrane to reduce symptoms associated with allergies and the common cold comprising (i) about 90-99.999 % w/w carrier, (ii) about 0.001 to about 5.0 % w/w oxymetazoline hydrochloride, (iii) about 0.00001 to about 5.0 % w/w of a permeation enhancer comprising liposomes, wherein the composition has a viscosity between about 2,500 to about 40,000 centipoise.

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in the obviousness-type double patenting section.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Haslwanter teaches aqueous nasal compositions comprising a therapeutic or palliative agent, water, and a mixture of microcrystalline cellulose, and alkali metal carboxyalkylcellulose, wherein in one embodiment the nasal spray exhibits a very rapid viscosity recovery upon removal of shear forces (title; abstract; Figure 1; col. 2, lines 16-32). Haslwanter's Examples 3D-3G (col. 6, line 50 through col. 7, line 13) disclose compositions comprising (a) **~88-95% w/w water (carrier), (b) 0.0488 % w/w oxymetazoline hydrochloride, (c) ~2.44-2.93 % w/w AVICEL-591 (an 89:11 mixture of microcrystalline cellulose and sodium carboxymethylcellulose; thickener), (d) about 0-3% w/w PVP, (e) about 0-4.9% PEG-32 (emulsion agent), (f) about 0.095 % w/w sodium phosphate dibasic (buffer), (g) about 0.54% w/w sodium phosphate dibasic (buffer), (h) about 0.029% w/w disodium EDTA (permeation enhancer, sequestering agent, and preservative), (i) about 0.14% w/w of a 17% aq. benzalkonium chloride solution (preservative), (j) about 0.24% w/w benzyl alcohol (preservative)**, and (k) about 0.146% w/w lemon flavor.

The compositions generally comprise **at least about 2.5% of cellulose/carboxyalkylcellulose mixture** (thickener), preferably about 2.5-3.5% w/w (col. 3, lines 56-64). The compositions generally have a pH of about 4 to about 8 and may comprise buffering substances, such as phosphate or citrate buffer systems (col. 4, lines 14-19). The compositions may also comprise up to 10% w/w, preferably 0.5-5% w/w of a rheology-modifying agent (i.e. thickener), such as sodium carboxymethyl cellulose, algin, **carageenans, hydroxypropyl cellulose, polyethylene glycols, dextran**, or combinations of two or more such agents (col. 4, lines 25-32). The composition **may further comprise additional humectants**

(e.g. glycerin [also known as glycerol], PEG, or other glycols), preservatives (e.g. benzyl alcohol, parabens, and benzalkonium chloride), and aromatic substances (e.g. camphor, menthol, and eucalyptol) (col. 4, lines 33-46). The amount of **cellulose/carboxyalkylcellulose mixture and other rheology modifiers can be varied to obtain a desired viscosity behavior** (col. 5, lines 10-15).

Sundgreen teaches that liposomes are conventional carriers [0206] and **that liposomes are expected to enhance penetration (i.e. enhance permeation) of active agent into the mucosa, such as the nasal mucosa** [0604].

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Haslwanter lacks the teaching of decongestant compositions comprising liposomes. This deficiency is cured by the teachings of Sundgreen. Haslwanter lacks the teaching of an explicit viscosity value for the invented compositions. The selection of a particular viscosity is obvious as explained below.

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been obvious to a person or ordinary skill in the art at the time of the instant invention to combine the teachings of Haslwanter and Sundgreen, because Haslwanter teaches nasal compositions that would benefit from the inclusion of mucosal/nasal penetration enhancers, such as liposomes. An ordinary skilled artisan would have been motivated to include liposomes in Haslwanter's invented compositions to enhance the uptake of the active ingredient

(e.g. oxymetazoline hydrochloride) present in Haslwanter's compositions. An ordinary skilled artisan would have had a reasonable expectation that the inclusion of liposomes would successfully enhance the permeation or penetration of active agent in Haslwanter's compositions, because the art explicitly suggests that liposomes would enhance penetration of active ingredient in mucosal tissues, such as nasal mucosa.

Regarding the composition viscosity, it is the Examiner's position that Haslwanter's invented compositions necessarily have a viscosity meeting the limitations of Applicants' claims 30-31, because the amount of thickener in Haslwanter's compositions is within the range disclosed by Applicants as corresponding to a viscosity range of about 2,500 cp to about 40,000 cp as evidenced by Applicants' claims 40 and 41. Furthermore, Haslwanter's exemplified compositions are characterized as being "no-drip", as evidenced by Haslwanter's Figure 1. Finally, it is art recognized that varying the amount of thickener and other rheology modifiers in a composition varies the compositions viscosity. Because the amount of a composition ingredient, such as a thickener, is a result effective parameter, viscosity is also a result effective parameter, wherein the amount of thickener is varied. Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because the combined teachings of the prior art is fairly suggestive of the claimed invention.

Claims 40-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haslwanter et al. (U.S. Patent No. 6,565,832) in view of Sundgreen et al. (U.S.

2002/0147232) as applied to claims 30-31 above, and further in view of Bates (U.S. Patent No. 4,826,683), as evidenced by Schulte (U.S. Patent No. 4,708,873).

Applicant Claims

Applicants claim a composition for application to a nasal membrane to reduce symptoms associated with allergies and the common cold comprising (i) about 90-99 % w/w water, (ii) about 0.045 to about 0.055 % w/w oxymetazoline hydrochloride, (iii) about 0.00001 to about 5.0 % w/w of a permeation enhancer, (iv) about 0 to about 1.0 wt % aromatic substance selected from the group consisting of camphor, eucalyptus oil, menthol, azulen, extracts thereof or mixtures thereof, (v) about 0.001 to about 1.0 % w/w preservative, (vi) about 0.000001 to about 5.0% w/w thickener, (vii) 0.05% to about 5.0% glycerin, (viii) about 0.00001 to about 1.0% w/w emulsion agent, and (ix) about 0.0002 to about 6.0% w/w buffer.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The teachings of Haslwanter and Sundgreen have been set forth above.

Bates teaches **decongestant compositions in the form of nasal spray** that are designed to be applied to the nasal passages comprising **about 0.1-5.0 g/L (i.e. ~0.0001-0.005% w/w) aloe vera (i.e. aloe barbadensis gel)**, about 10-1,000 mg/L vitamin C (i.e. ~0.00001-0.001 % w/w), zinc, carriers, solvent, etc. (title; abstract; col. 1, lines 1-6 and 55-68; col. 2, lines 48-64; and claims 1-7). The aloe in Bates' compositions is either aloe juice or aloe vera gel, **preferably aloe vera gel**.

Schulte teaches that aloe vera stimulates wound healing and inhibits the formation of granulation tissue (col. 1, lines 53-57).

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Haslwanter lacks the teaching of decongestant compositions comprising aloe barbadensis gel. This deficiency is cured by the teachings of Bates. Haslwanter lacks the teaching of compositions comprising hydroxyethylcellulose. Hydroxyethyl cellulose is a well-known conventional thickener, as admitted by Applicants (see page 6 of Applicants' remarks submitted 7/30/08, which is the 1st page of Applicants' arguments).

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been obvious to a person or ordinary skill in the art at the time of the instant invention to modify the compositions of Haslwanter to include aloe vera gel (i.e. aloe barbadensis gel), because aloe vera gel is a conventional ingredient in nasal spray formulations (Bates) that promotes healing (Schulte). An ordinary skilled artisan would have been motivated to include aloe vera gel in Haslwanter's invented compositions, because it is a conventional ingredient in nasal formulations that can also stimulate healing. An ordinary skilled artisan would have had a reasonable expectation of successfully preparing nasal spray compositions comprising aloe vera gel, because aloe vera gel is a conventional ingredient of nasal spray compositions and nasal spray compositions comprising aloe vera gel are known.

Regarding the composition viscosity, it is the Examiner's position that Haslwanter's invented compositions necessarily have a viscosity meeting the limitations of Applicants' claims 41-47, because the amount of thickener in Haslwanter's compositions is within the range disclosed by Applicants as corresponding to a viscosity range of about 2,500 cp to about 40,000 cp as evidenced by Applicants' claims 40 and 41. Furthermore, Haslwanter's exemplified compositions are characterized as being "no-drip", as evidenced by Haslwanter's Figure 1. Finally, it is art recognized that varying the amount of thickener and other rheology modifiers in a composition varies the compositions viscosity. Because the amount of a composition ingredient, such as a thickener, is a result effective parameter, viscosity is also a result effective parameter, wherein the amount of thickener is varied. Finally, regarding the amounts of the other composition ingredients (e.g. buffering compounds), the amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient needed to achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, the optimization of ingredient amounts would have been obvious at the time of applicant's invention. Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because the combined teachings of the prior art is fairly suggestive of the claimed invention.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. AFRIN® No Drip 12 hr Relief is a commercially available product sold by Schering-Plough based in part on Haslwanter (6,565,832) and U.S. Patent Nos. 6,481,146 and 6,316,483. AFRIN® No Drip 12 hr Relief comprises 0.05% w/w oxymetazoline hydrochloride as the active ingredient and various inactive ingredients, such as benzalkonium chloride, benzyl alcohol, camphor, edetate disodium, eucalyptol, menthol, PEG, water, phosphate buffer, etc. AFRIN® is a commercially available product that has been available on sale since at least 1993 (Drug Information Handbook, Lexi-Comp, Inc. Cleveland, pp 675-676). The product 4-Way® (1995 Physician's Desk Reference, 49th edition, Medical Economics Data Production Company: Montvale, NJ, 1995, pp 705) is an aqueous nasal spray comprising 0.05% w/w oxymetazoline hydrochloride, buffer, glycine, sorbitol, benzalkonium chloride, and phenylmercuric acetate. VICK's® Sinex 12-hour Nasal Spray is another commercial product comprising 0.05% w/w oxymetazoline hydrochloride as the active ingredient and various inactive ingredients, such as, benzalkonium chloride, camphor, clorhexidine gluconate, disodium EDTA, eucalyptol, menthol, PEG, water, potassium phosphate, etc

Claims 30-31 and 40-57 are rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571) 272-5548. The examiner can normally be reached on M-F, 9:00-6:30, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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